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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/679,875	**Applicant(s)** KURTZMAN ET AL.	
	Examiner Anne Marie S. Wehbe	**Art Unit** 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4 are pending and under in the instant application. An action on the merits follows.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows. In the preliminary amendment filed on 10/15/03, the applicant amended the paragraph on page 1, at line 10, which details the claims of priority to various parent applications. However, it is noted that the amended paragraph states that this application is a continuation of 09/858,728. The disclosure presented in a continuation must be the same as that of the original application; i.e., the continuation should not include anything which would constitute new matter if inserted in the original application. The specification of the 09/858,728 application does not provide support for HIV virus antigens, or more specifically disclose the HIV envelope protein or subunits gp120 and p24 of the envelope protein. As such, the instant application constitutes a continuation-in-part of parent application 09/858,728. The applicant is required to amend the specification to indicate that the instant application is a continuation-in-part application in order to perfect priority to the parent application. In addition, since applicant's preliminary amendment was filed, parent application 09/858,728 issued as U.S. Patent No. 6,710,036 on March 23, 2004. The applicant is required to amend the specification to update the current status of the 09/858,728 application.

It is further noted that under 35 U.S.C. 120, a claim in a U.S. application is only entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph, in the earlier filed application. See, e.g., *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 47 USPQ2d 1829 (Fed. Cir. 1998); *In re Scheiber*, 587 F.2d 59, 199 USPQ 782 (CCPA 1978). In view of the disclosure present in parent applications 09/858,728, 09/121,162, and 60/053,733, the office acknowledges that claim 1 has benefit of priority to the filing dates of the parent applications. However, as the subject matter of claims 2-4 is not disclosed in the parent applications, see above, the effective filing date for the subject matter of claims 2-4 is the filing date of the instant application, 10/15/03.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,242,426 (6/5/01), hereafter referred to as the '426 patent. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. Instant claim 1 recites a method of eliciting an immune response in a mammalian subject comprising providing a recombinant AAV virion containing a nucleic acid molecule encoding an AIDS virus antigen operably linked to expression control sequences and introducing said recombinant AAV into a recipient cell of a mammalian subject such that expression of the AIDS virus antigen elicits an immune response to said antigen in the subject. Claims 1-8 of the '426 patent recite broad methods of eliciting immune responses to an antigen comprising providing a recombinant AAV virion containing a nucleic acid molecule encoding an antigen operably linked to expression control sequences and introducing said recombinant AAV into a recipient cell of a mammalian subject such that expression of the antigen elicits an immune response to said antigen in the subject. Claim 5 of the '426 patent specifically recites wherein the antigen is a viral antigen. Instant claim 1 is therefore a species of the broader claims in the '426 patent. However, while the claims in the '426 patent, and particularly claim 5, do not specifically recite an AIDS virus antigen, the specification of the '426 patent clearly teaches that viral antigens for use in the instant methods include those derived from the causative agents of diseases including AIDS ('426 specification, columns 24-25, bridging paragraph). Thus, the claims of the '426 patent encompass instant claim 1 and the specification provides specific motivation for using an AIDS virus antigen. As such, claims 1-8 of the '426 patent render instant claim 1 obvious.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The applicant claims a method of eliciting an immune response in a mammalian subject comprising the introduction of a recombinant AAV virion containing a nucleic acid molecule encoding the p24 subunit of the HIV envelope protein. While the term HIV envelope protein and the p24 subunit of the HIV envelope protein are present in the claims filed with the application, the specification does not specifically teach or disclose the HIV virus, the envelope protein of HIV, or the p24 subunit of the HIV envelope protein. Page 40 of the specification contains the only reference to AIDS where it recites that a suitable viral antigen will be derived from the causative agents of diseases which include AIDS. The specification fails to actually identify any virus which is known as the causative agent of AIDS, or particularly identify any antigen derived from the HIV virus let alone provide guidance as to the physical, chemical, or structural properties of any viral antigen associated with AIDS. More specifically, the specification does not provide any guidance as to the physical, structural, or functional properties of a p24 subunit of HIV envelope or provide guidance as to a nucleic acid encoding the p24 subunit of the HIV envelope protein. The envelope protein from HIV, also known in the art as gp160, was known to be composed to two subunits, gp120 and gp41 (see for instance

Chatterjee et al. (1992) Pathobiology, Vol. 60 (4), 181-186). The art does not teach or suggest any subunit of HIV envelope referred to as p24. In the HIV literature, p24 is the gag protein (Chatterjee et al., page 181). Therefore, since the art at the time of filing to the present does not teach a p24 subunit of HIV envelope, and the specification is silent in regards to the properties or characteristics of a p24 subunit of HIV envelope, the specification fails to provide an adequate written description for the p24 subunit of HIV envelope.

Case law states that, "simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus" *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (CA FC 1996). Thus, in the instant application, a statement that any viral antigen associated with a disease or AIDS made in the specification is not sufficient to satisfy the written description requirement for HIV envelope protein, and in particular the p24 subunit of HIV envelope. Furthermore, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). In the absence of any description of the HIV envelope p24 polypeptide or nucleic acid encoding the polypeptide, or any description of the specific properties of these molecules that define their biological activity, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides which may encode the p24 subunit of the HIV envelope. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Thus, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for the p24 subunit of HIV envelope. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention as claimed. Specifically, the specification does not provide enablement for methods of generating a therapeutic or prophylactic immune responses in a mammal by administering a recombinant AAV virion encoding any AIDS virus antigen using any route of administration.

The specification fails to provide sufficient guidance for AIDS virus antigens, the HIV envelope, and particularly the p24 subunit of HIV envelope. As noted above, the specification fails to actually disclose any particular "AIDS virus" or any viral antigen associated with AIDS. The specification does not disclose HIV or disclose nucleic acids encoding HIV envelope or any other HIV antigen. In particular, the specification does not teach a p24 subunit of the HIV envelope. As noted in the written description rejection above, the specification does not provide any guidance as to the physical, structural, or functional properties of a p24 subunit of HIV envelope or provide guidance as to a nucleic acid encoding the p24 subunit of the HIV envelope protein. The envelope protein from HIV, also known in the art as gp160, was known to be composed to two subunits, gp120 and gp41 (Chatterjee et al., supra, pages 181-186). The art does not teach or suggest any subunit of HIV envelope referred to as p24. In the HIV literature, p24 is the gag protein (Chatterjee et al., supra, page 181, abstract). Therefore, since the art at the time of filing to the present does not teach a p24 subunit of HIV envelope, and the specification is silent in regards to the properties or characteristics of a p24 subunit of HIV envelope, it would have required undue experimentation for the skilled artisan to identify a p24 subunit of the HIV envelope and use it applicant's claimed methods.

The specification further fails to provide an enabling disclosure for generating any type of immune response against any AIDS virus antigen using the disclosed methods. The specification's working examples disclose an rAAV vector encoding the model tumor antigen ovalbumin operatively linked to the CMV-IE promoter/enhancer (rAAV-Ova). The working examples demonstrate that injection of rAAV-Ova intramuscularly, intravenously, intraperitoneally (i.p.), or subcutaneously into C57BL/6 mice results in the generation of detectable levels of Ova-specific CTL and anti-Ova IgG antibodies. However, Ova, chicken ovalbumin, is not an AIDS virus antigen. Further, the working examples which demonstrate the generation of immune responses against a single antigen, Ova, cannot be correlated with the generation of immune responses against other types of antigens, including AIDS virus antigens or HIV envelope in particular. At the time of filing, the prior art teaches the use of rAAV vectors over other types of viral vectors for the delivery and stable expression of therapeutic genes in primarily non-dividing cells for the specific reason that adeno-associated viral vectors, unlike adenoviral or retroviral vectors, do not elicit damaging anti-viral immune responses. The art reports that the complete lack of anti-viral CTL and minimal antibody response results in the sustained expression of AAV encoded genes for up to 6 months or longer in some types of cells such as muscle cells and neurons (Xiao et al. (1997) Exp. Neurol., Vol. 144, 113-124). Specifically, the art at the time of filing teaches the lack of specific cellular immune responses in non-human mammals such as monkeys, rabbits, mice and rats, against vector encoded genes including the bacterial antigen LacZ, and the xenoantigens human erythropoietin, CFTR, and factor IX (Xiao et al., *supra*, Kessler et al. (1996) Proc. Natl. Acad. Sci., Vol. 93, 14082-14087, and Jooss et al. (1998) J. Virol., Vol. 72 (5), 4212-4223). Jooss et al., in particular, demonstrates that whereas mice injected with an adenoviral vector encoding LacZ develop LacZ specific CTL, generate both Th1 and Th2 type cytokine secreting cells, and generate significant titers of anti-LacZ antibodies, mice injected with AAV-LacZ do not (Jooss et al., *supra*, pages 4214-4215, Figure 2 and Tables 2+3). Jooss et al. also teaches that the lack of a LacZ specific immune response is not the result of immune tolerance to LacZ but rather LacZ unresponsiveness (Jooss et al., *supra*, page 4217, column 1, paragraph 1). Thus, the art at the time of filing establishes that numerous proteins expressed by rAAV do not in fact generate immune responses in vivo. As such, the skilled artisan would not have been able to predict whether the administration of recombinant AAV encoding and AIDS virus antigen or HIV envelope in particular would be capable of generating an immune response in vivo without undue experimentation.

The specification further does not provide an enabling disclosure for generating prophylactic or therapeutic immune responses by administering by any route a recombinant AAV encoding any "AIDS" virus antigen. Please note that the specification clearly teaches that the purpose for generating immune responses against pathogenic antigens is for the treatment of disease, in this case AIDS. At the time of filing the prior art identifies several factors which significantly affect the generation of immune responses to an antigen which include, genetics, dose or concentration of antigen, and route of antigen administration (Abbas et al. (1996) Nature, Vol. 383, 787-793, and Golding et al. (1994) Am. J. Trop. Med. Hyg., Vol. 50 (4), 33-40). The prior art teaches that the concentration of antigen significantly affects the development of cellular (Th1) versus humoral(Th2) immune responses such that low antigen concentrations preferentially induce Th1 type responses and high concentrations of antigen induce Th2 type responses (Abbas et al., *supra*). A further complicating factor is the genetic background of the infected mammal. The prior art contains numerous reports which demonstrate the Balb/C mice versus C57Bl/6 mice develop different responses to various pathogens. The nature and route of administration of the antigen is also of concern to the generation of a particular T helper phenotype. Golding et al. teaches that intravenous or intraperitoneal immunization leads to preferential induction of Th1 cells whereas subcutaneous or intramuscular immunization leads to Th2 cells which may be attributable to the participation of various antigen-presenting cells (Golding et al., *supra*). Thus, the art at the time of filing clearly teaches that a significant number of variables affect the generation of specific immune responses which render the generation of a particular type of immune response in any mammal unpredictable for any given antigen.

Furthermore, the strength and nature of the immune response generated by a particular antigen was known at the time of filing to be critical to its ability to successfully protect against infection. A weak immune response, or an immune response that only generates antibodies and no CTL may be insufficient to protect against many pathogens. In the case of pseudorabies virus, Monteil et al. discloses that the immunization of naive one-day-old piglets with a plasmid DNA encoding the gene for the gD glycoprotein induces antibodies which do not protect the piglets from PRV challenge (Monteil et al. (1996) Veterinary Research, Vol. 27 (4-5), page 443, abstract). Yasutomi et al. further teaches that immunization of rhesus monkeys with a live viral vector which encodes the SIV gag protein generates a non-protective CTL response, but fails to generate a humoral immune response despite the presence of MHC class II and antibody binding epitopes in the gag protein (Yasutomi et al. (1995) J. Virol., Vol. 69 (4), page 2279, abstract). In addition, Yasutomi et al. teaches that while boosting vaccinated animals with a gag peptide/liposome complex significantly increases the anti-gag CTL response, it still did not provide increased protection against SIV challenge (Yasutomi et al., *supra*, abstract). As to immunization of humans against latent infectious agents such as HIV, Fox in a review of the "First National Conference on Human Retroviruses and Related Infections" summarizes the conference's central theme as, "no therapy has emerged as a sure winner in the campaign against HIV, not a preventive vaccine nor a therapeutic vaccine nor any of the immune-system-boosting treatments" (Fox (1994) Bio/Technology, 12, 128). Furthermore, Klein et al. in a review of the challenges facing the development of HIV vaccines states, " A fundamental question in HIV vaccine research is what factors correlate strongly with protective immunity or prevent the progression to AIDS. The answer is still unknown", " The results of studies in animals and humans are inconclusive about what factors correlate with what kinds of protection", and, "The likely composition of a successful HIV vaccine is still unknown, primarily because the factors involved in immunity that must be targeted by the vaccine are still unclear" (Klein et al. (2000) Clinical Therapeutics, Vol. 22 (3), 295-314, see pages 303 and 310 in particular). Thus, the art at the time of filing demonstrates the unpredictability in generating therapeutic or prophylactic immune responses against viruses, in particular immunodeficiency viruses such as SIV and HIV, by genetic immunization.

Therefore, based on the art recognized unpredictability of generating therapeutic immune responses against HIV, the unpredictability of using AAV virions to generate immune responses against protein in vivo, the variability in immunogenicity between different proteins based on their structure and cellular location, the nature of various types of antigens and their associated diseases, and the breadth of the claims, it would have required undue experimentation for the skilled artisan at the time of filing to practice applicant's invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As discussed in detail above, neither the specification nor the prior art describes or teaches a p24 subunit of HIV envelope. As such, the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in—
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
>
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2003/0147912 (8/7/02), hereafter referred to as Johnson. The applicant claims a method of eliciting an immune response in a mammalian subject comprising providing a recombinant AAV virion containing a nucleic acid molecule encoding an AIDS virus antigen operably linked to expression control sequences and introducing said recombinant AAV into a recipient cell of a mammalian subject such that expression of the AIDS virus antigen elicits an immune response to said antigen in the subject. The applicant further claims said methods wherein the AIDS virus antigen is HIV envelope.

Johnson teaches methods for immunizing a host against HIV by administering a vaccine composition comprising a recombinant AAV genome encoding an immunodeficiency virus protein operably linked to promoter and polyadenylation sequences, wherein the protein is the HIV envelope protein (Johnson et al., pages 12-13, claims 1-20, and particularly claims 2 and 20, and also page 2 and the abstract). Thus, by teaching all the limitations of the claims as written, Johnson anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 3 is rejected under 35 U.S.C. 103(a) as being obvious over US 2003/0147912 (8/7/02), hereafter referred to as Johnson, in view of Guan et al. (2000) Chinese J. Exp. Clin. Virol., Vol. 14 (4), 322-324. The applicant claims a method of eliciting an immune response in a mammalian subject comprising providing a recombinant AAV virion containing a nucleic acid molecule encoding an AIDS virus antigen operably linked to expression control sequences and introducing said recombinant AAV into a recipient cell of a mammalian subject such that expression of the AIDS virus antigen elicits an immune response to said antigen in the subject, wherein the AIDS virus antigen is the gp120 subunit of HIV envelope.

Johnson teaches methods for immunizing a host against HIV by administering a vaccine composition comprising a recombinant AAV genome encoding an immunodeficiency virus protein operably linked to promoter and polyadenylation sequences, wherein the protein is the HIV envelope protein (Johnson et al., pages 12-13, claims 1-20, and particularly claims 2 and 20, and also page 2 and the abstract).

While Johnson teaches methods of immunizing by administering recombinant AAV encoding HIV envelope, Johnson does not specifically teach to use the gp120 subunit of HIV. Guan et al. supplements Johnson by teaching a recombinant AAV encoding the gp120 subunit of HIV envelope (Guan et al., pages 322-323). Guan et al. further provides motivation for using the gp120-AAV for generating anti-HIV immune responses by teaching the use of the recombinant AAV encoding gp120 as a vaccine (Guan et al., page 322, abstract, and page 324). Thus, in view of the motivation to use the gp120 subunit of HIV envelope encoded by a recombinant AAV as a vaccine as taught by Guan et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the recombinant AAV encoding gp120 for the recombinant AAV encoding HIV envelope in the methods of immunizing taught by Johnson. Further, the skilled artisan would have had a reasonable expectation of success in generating immune responses against gp120 expressed by AAV based on the demonstration by Johnson et al. that recombinant AAV successfully infects and expresses protein in mammalian cells in vitro and in vivo.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER